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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
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09/599,452 06/22/00 BLOOM

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EXAMINER

DAVIS, K

ART UNIT

PAPER NUMBER

1636

DATE MAILED:

08/13/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

| | | |
|------------------------------|--------------------|--------------|
| Office Action Summary | Application No. | Applicant(s) |
| | 09/599,452 | BLOOM ET AL. |
| | Examiner | Art Unit |
| | Katharine F. Davis | 1636 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 22 June 2000.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-41 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 1-41 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
 If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

1. Certified copies of the priority documents have been received.

2. Certified copies of the priority documents have been received in Application No. _____.

3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) Notice of References Cited (PTO-892) 4) Interview Summary (PTO-413) Paper No(s). _____.

2) Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) Notice of Informal Patent Application (PTO-152)

3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5. 6) Other: _____.

DETAILED ACTION

This Office Action is in response to the application filed on June 22, 2000. Claims 1-41 are pending in the instant application.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: it is incomplete. The oath claims priority to a PCT application without an application number. Additionally, the oath claims the PCT as a foreign document under 35 U.S.C. 119(a)-(d). This is not permitted since the oath also claims benefit under 35 U.S.C. 119(e) to a US provisional application (60/139,889) that was filed **prior to** the PCT document.

Drawings

The drawing filed on June 22, 2000 has been approved by the draftsperson.

Claim Objections

Claims 5 and 8 are objected to because of the following grammatical informalities: Claim 5 lacks a comma separating BRL3781 and BRL3784. Appropriate correction is required.

Claim 8 recites "... is and *E. coli*." This objection may be overcome by amending the claim to read "...is **an** *E. coli*."

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 1 is rejected under 35 U.S.C. 101 because it is directed to non-statutory subject matter. Claim 1 reads on microorganisms that are naturally occurring. For example, *Streptomyces coelicolor* is a rapid growing species of bacteria that lacks endogenous plasmids (see US Patent 6,215,007 B1, column 15, lines 24-25). Products of nature are not patentable. Amending the claim to read "**An isolated** rapid growing microorganism..." would overcome this rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 6, 7, 11, 14-16, 20, 22, 23 and 27-39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the rapidly growing strains of *E. coli* listed in Table I, does not reasonably provide enablement for **any** rapidly growing microorganism. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1, 2, 6, 7, 11, 14-16, 20, 22, 23 and 27-39 are drawn to a rapid growing microorganism and use of the said rapid growing microorganism in methods for cloning and producing a protein of interest. The rapid growing microorganism can be of the genus *Escherichia*. Claims 27-33 are further drawn to kits comprising the said rapid growing microorganism and/or reagents for carrying out the methods of use of the said rapid growing microorganism.

The following factors have been considered in formulating this rejection (*In re Wands*, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)): the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction or guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.

The instant claims are broad in that they encompass any rapid growing microorganism, a method(s) of cloning any nucleic acid molecule using any recombinant vector by transforming any rapid growing microorganism and a method of producing any protein by transforming any rapid growing microorganism with any recombinant vector(s).

The nature of the invention is a method of making a rapid growing microorganism for use in cloning in order to increase the efficiency of the cloning method.

The relative skill of those in the art of molecular biology (culture of microorganisms, cloning and protein expression) is high.

The area of the invention is unpredictable. As indicated above any type of microorganism can be considered rapid growing, thus one of skill in the art could not predictably ascertain what type of microorganism would be an appropriate "starting strain" for use in the claimed methods of cloning and protein expression. One of skill in the art would know how to cure a microorganism of endogenous plasmids. However culture conditions differ depending on the type of microorganism. Is one set of culture parameters ideal to support all types of rapidly growing microorganisms? Or would one set of culture parameters be growth inhibiting to certain microorganisms while the same parameters induce growth in other microorganisms?

The instant specification provides little direction or guidance to support the claimed invention. The specification defines a rapid growing microorganism as having an increased growth rate, greater than 5%-200% of the growth of a reference microorganism (see page 12, lines 18-21). There is no definitive reference microorganism nor is there defined culture conditions for ascertaining increased growth of any microorganism.

The working examples use only strains and/or derivatives of *E. coli* W and no other microorganism.

The quantity of experimentation necessary to carry out the claimed invention is high as the skilled artisan could not rely on the prior art or the instant specification to teach how to make and/or use any rapid growing microorganism in the claimed methods. In order to determine what type of microorganism would be appropriate for use in the claimed methods one of skill in the art would have to ascertain defined parameters for determining rapid growth of any microorganism. Since neither the prior art nor the instant specification provides the answer to this question it would require a large quantity of trial and error experimentation by the skilled artisan to answer this question and successfully make and/or use (in the claimed methods of cloning and/or protein expression) the claimed microorganisms.

Based on the broad scope of the claims, the nature of the invention, the skill of those in the art, the unpredictability of the area of the invention, the lack of sufficient guidance or working examples in the specification and the quantity of experimentation necessary, it would clearly require undue experimentation by one of skill in the art to use any rapid growing microorganism in the claimed cloning and/or protein expression methods.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "rapid growing" in claims 1-41 is a relative term which renders the claims indefinite. The term "rapid growing" is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The instant specification defines a rapid growing microorganism as having an increased growth rate, a growth rate that is 5%-200% increased as compared to a reference microorganism. There is no definitive reference microorganism nor is there defined culture conditions for ascertaining increased growth of a microorganism. Thus, any microorganism can be considered rapid growing.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Khosla *et al.* (Molecular Microbiology 6(21):3237-3249 1992). Khosla *et al.* disclose a strain of bacteria, *Streptomyces coelicolor*, that is a rapid growing microorganism lacking endogenous plasmids (see page 3239, under Results). Claim 1 reads on the microorganism disclosed by Khosla *et al.*

Claims 1-3 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Bharathi *et al.* (FEMS Microbiology Letters 84:37-40 1991, IDS Reference AS1). Bharathi *et al.* disclose a strain of *Escherichia coli* 393 (see Table 2, page 39) that lacks endogenous plasmids and a method of making said strain. The 393 strain of *Escherichia coli* was treated with the curing agent Hexamine ruthenium (III) chloride (HRC). The instant claims 1-3 do not require that the rapid growing microorganism be naturally lacking endogenous plasmids. Claims 1-3 and 20 read on the 393 strain of *Escherichia coli* and the method of making said strain disclosed by Bharathi *et al.*

Claims 6-8, 11 and 22-24 are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent 4,966,841 (Riley). Riley discloses a method of cloning enhancer fragments comprising the steps of constructing a population of recombinant cloning vectors, transforming an *Escherichia coli* host strain with the recombinant cloning vectors and selecting the transformed *Escherichia coli* cells containing the recombinant vector (see columns 4-6, Isolation and Cloning of Growth Enhancing Fragments and also Examples 1 and 2). The *E. coli* cells of Riley take up the recombinant plasmid so therefore are competent cells for the uptake of exogenous DNA (see Table 1, column 8). The recombinant vectors (plasmids) of Riley are then isolated from the transformed *E. coli* cells (see columns 6-7, Assays of Plasmid Recovery). The *E. coli* host strain selected by Riley is considered to be capable of rapid growth (see column 6, lines 12-18). Thus, claims 6-8, 11 and 22-24 read on the methods and host strains of Riley.

Claims 15-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Bhandari *et al.* (Journal of Bacteriology 179:4403-4406 1997, IDS Reference AR1). Bhandari *et al.* disclose a method of producing proteins (rat protein tyrosine phosphatase, *E. coli* DNA polymerase I and *E. coli* SSB protein, see figure 2, page 4404) by transformation of *Escherichia coli* host cells (strain GJ1158) with recombinant vectors encoding a gene(s) for the protein. *E. coli* is considered to be a microorganism capable of rapid growth. Thus, claims 15-17 read on the methods and host strains of Bhandari *et al.*

Claims 34-37, 39 and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent 4,981,797 (Jessee *et al.*). Jessee *et al.* disclose a composition comprising rapid growing microorganisms (*Escherichia coli*, see column 5, lines 10-19). The composition of Jessee *et al.* can include a transformation buffer comprising glycerol and buffering salts (see column 4, lines 44-47). Jessee *et al.* also disclose a method of making *E. coli* cells competent (see abstract and through out entire patent). Thus, claims 34-37, 39 and 40 read on the composition and methods of Jessee *et al.*

Conclusion

Claims 1-41 are rejected. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Katharine F. Davis whose telephone number is (703) 605-1195 with direct desktop RightFax (703) 746-5199. The examiner can normally be reached on Monday-Friday (8:30am-5:00pm). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Schwartzman can be reached on (703) 308-7307. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-1935 for After Final communications. Any inquiry concerning the formalities of this application should be

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directed to Patent Analyst Dianiece Jacobs whose telephone number is (703) 305-3388. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Katharine F. Davis
August 13, 2001

DAVID GUZO
PRIMARY EXAMINER
